

## CLAIMS

1. An agent for therapy and/or prevention of kidney diseases, comprising as an effective ingredient a substance which inhibits casein kinase 2.
2. The agent for therapy and/or prevention of kidney diseases according to claim 1, wherein said casein kinase 2 is originated from cells constituting kidney.
3. The agent for therapy and/or prevention of kidney diseases according to claim 1 or 2, wherein said substance is a substance which inhibits  $\alpha$  subunit and/or  $\alpha'$  subunit of casein kinase 2.
4. The agent for therapy and/or prevention of kidney diseases according to any one of claims 1 to 3, wherein said substance is (1) a substance which inhibits expression of casein kinase 2, or (2) a substance which inhibits enzyme activity of casein kinase 2.
5. The agent for therapy and/or prevention of kidney diseases according to claim 4, wherein said substance which inhibits expression of casein kinase 2 is a nucleic acid molecule that inhibits expression of casein kinase 2.
6. The agent for therapy and/or prevention of kidney diseases according to claim 5, wherein said nucleic acid molecule which inhibits expression of casein kinase 2 is an antisense oligonucleotide that targets mRNA coding for casein kinase 2, and that can inhibit expression of casein kinase 2.
7. The agent for therapy and/or prevention of kidney diseases according to claim 6, wherein said antisense oligonucleotide has 12 to 50 bases having a sequence selected from the group consisting of coding regions, 3'-untranslated regions, 5'-untranslated region, 5' cap and intron/exon junctions of mRNA coding for casein kinase 2.
8. The agent for therapy and/or prevention of kidney diseases according to claim 7, wherein said nucleic acid molecule of said antisense oligonucleotide against casein kinase 2 is an S-oligonucleotide.
9. The agent for therapy and/or prevention of kidney diseases according to claim 7 or 8, wherein said nucleic acid molecule forming said antisense oligonucleotide against

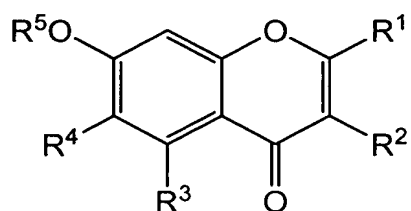
casein kinase 2 has a sequence shown in any one of SEQ ID NOs: 1-10.

10. The agent for therapy and/or prevention of kidney diseases according to claim 9, wherein said antisense oligonucleotide against casein kinase 2 has a sequence shown in SEQ ID NO: 1.

11. The agent for therapy and/or prevention of kidney diseases according to claim 4, wherein said substance which inhibits casein kinase 2 is a compound that inhibits enzyme activity of casein kinase 2.

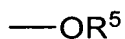
12. The agent for therapy and/or prevention of kidney diseases according to claim 11, wherein said compound which inhibits enzyme activity of casein kinase 2 is a compound that inhibits enzyme activity of casein kinase 2 by not less than 30% in a range of concentration of 1 pM to 100  $\mu$ M.

13. The agent for therapy and/or prevention of kidney diseases according to claim 12, wherein said compound which inhibits enzyme activity of casein kinase 2 is



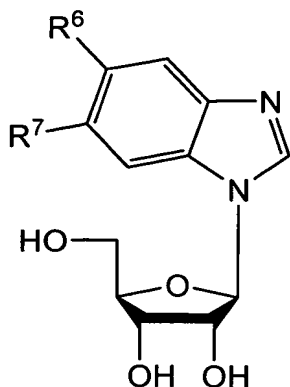
Formula I

(wherein  $R^1$  and  $R^2$  independently represent hydrogen, hydroxy or phenyl which may have one or more substituents selected from those represented by Formula 2, with the proviso that at least one of  $R^1$  and  $R^2$  is said phenyl group which may have said substituent(s);  $R^3$  and  $R^4$  independently represent hydrogen or a substituent represented by Formula 2; and  $R^5$  represents hydrogen, sugar residue,  $C_1$ - $C_4$  alkyl or acyl);



Formula 2

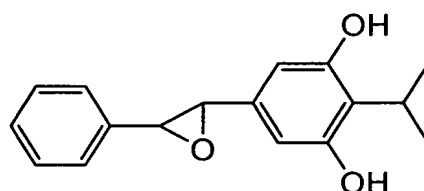
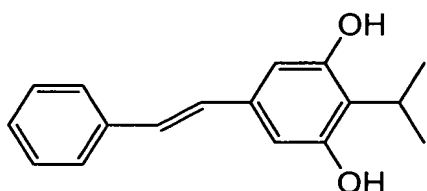
(wherein  $R^5$  represents the same meanings as  $R^5$  in Formula 2);



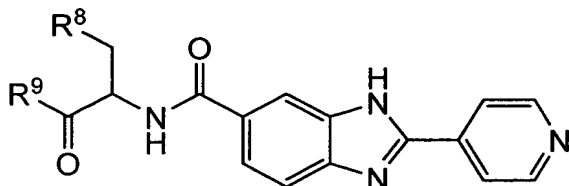
Formula 3

(wherein  $R^6$  and  $R^7$  independently represent hydrogen, halogen or  $C_1$ - $C_4$  alkyl);

TBB which is 4,5,6,7-tetrabromobenzimidazole; DRB which is 5,6-dibromo-1-( $\beta$ -D-ribofuranosyl)benzimidazole;

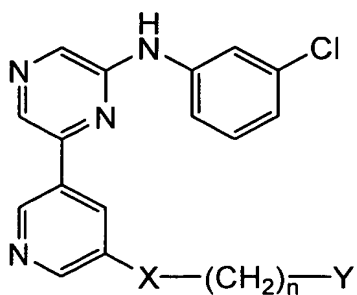


or



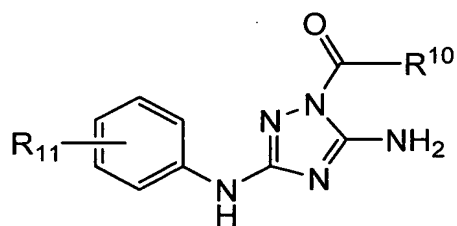
Formula 4

(wherein  $R^8$  represents phenyl which may be substituted by 1 to 3 substituents selected from halogens, methyl, trifluoromethyl and hydroxy, or quinolyl, ethylmethyl sulfide, t-butylphenylthio or N-ethylphenylamino; and  $R^9$  represents hydroxy or amino);



Formula 5

(wherein n represents 1 to 3; X represents -NH- or -CONH-; and Y represents hydroxy, piperidine, pyrrolidine, piperazine, pyrazole or triazole);



Formula 6

(wherein  $R^{10}$  represents 2-thienyl or phenyl which may be substituted by halogen, methyl, ethyl or t-butyl; and  $R^{11}$  represents  $-\text{SO}_2-\text{NH}_2$ ,  $-\text{SO}_2-\text{NHMe}$  or  $-\text{SO}_2-\text{NH}[(\text{CH}_2)_2\text{N}(\text{CH}_3)_2]$ , or a pharmaceutically acceptable salt thereof.

14. The agent for therapy and/or prevention of kidney diseases according to claim 13, wherein said substance which inhibits casein kinase 2 is a compound represented by the above-described Formula 1 (definitions of substituents are the same as described above) or a pharmaceutically acceptable salt thereof.

15. The agent for therapy and/or prevention of kidney diseases according to claim 14, wherein in the Formula 1,  $R^1$  is hydrogen or phenyl which may have one or two substituents selected from those shown represented by Formula 2;  $R^2$  is hydrogen or hydroxy; and  $R^5$  is hydrogen.

16. The agent for therapy and/or prevention of kidney diseases according to claim 15, wherein said substance which inhibits casein kinase 2 is apigenin.

17. The agent for therapy and/or prevention of kidney diseases according to any one of claims 1 to 16, wherein said kidney disease is glomerular nephritis, interstitial nephritis, nephrosclerosis, diabetic nephropathy or chronic or acute renal failure.

18. The agent for therapy and/or prevention of kidney diseases according to any one of claims 1 to 16, wherein said kidney disease is a nephritis other than one resulted from diabetes, or said kidney disease is characterized by increase in expression of casein kinase 2 or increase in enzyme activity of casein kinase 2.

19. Use of said substance which inhibits casein kinase 2 according to any one of claims 1 to 18 for the production of an agent for therapy and/or prevention of kidney diseases.
20. A method for therapy and/or prevention of kidney diseases, comprising administering an effective amount of said substance which inhibits casein kinase 2 according to any one of claims 1 to 18 to a patient or an animal suffering from a kidney disease, or to human or an animal for which prevention of a kidney disease is desired.
21. A method for diagnosis of kidney diseases, comprising measuring activity and/or content of casein kinase 2, and/or measuring expression amount of casein kinase 2 gene in a sample separated from body.
22. The method according to claim 21, wherein said sample is cells constituting kidney.
23. The method according to claim 21 or 22, wherein said casein kinase 2 is  $\alpha$  subunit and/or  $\alpha'$  subunit.
24. The method according to any one of claims 21 to 23, wherein said kidney disease is glomerular nephritis, interstitial nephritis, nephrosclerosis, diabetic nephropathy or chronic or acute renal failure.
25. The method according to any one of claims 21 to 23, wherein said kidney disease is a nephritis other than one resulted from diabetes, or said kidney disease is characterized by increase in expression of casein kinase 2 or increase in enzyme activity of casein kinase 2.
26. The method according to any one of claims 21 to 25, comprising measuring expression amount of casein kinase 2 gene.
27. An oligonucleotide having a nucleotide sequence complementary to a region in sense chain or antisense chain of casein kinase 2 gene, which is used for the method according to claim 26.
28. The oligonucleotide according to claim 27, which is a primer for gene

amplification or a probe for detecting gene.